

Amendments to the Specification:

Please insert the Sequence Listing following the Drawings.

Please delete paragraph [0301] on page 107 and replace it with the following paragraph:

[0301] N-terminal sequencing was carried out using an Applied Biosystems, Inc. (ABI) 447A automatic protein sequencer. Each sample was loaded onto a glass fiber disc, which had been placed in the sequencer and pre-cycled once. Following the pre-cycling step, a number of cycles of Edman degradation were performed using a standard protein sequencing program from ABI. The results are reported as the major phenylthiohydantoin (PTH)-amino acid detected for each cycle. (Standard one-letter designations for the 20 commonly occurring amino acids are used to report the resulting sequences. They are: A = alanine; C = cysteine; D = aspartic acid; E = glutamic; F = phenylalanine; G = glycine; H = histidine; I = isoleucine; K = lysine; L = leucine; M = methionine; N = asparagine; P = proline; Q = glutamine; R = arginine; S = serine; T = threonine; V = valine; W = tryptophan; Y = tyrosine.)

Results:

Trastuzumab:

Trastuzumab Form	Antibody Chain	N-terminal sequence
Crystalline	Heavy	E-V-Q-L-V-G-S (SEQ ID NO:1)
Crystalline	Light	D-I-Q-M-T-Q-S(SEQ ID NO:2)
Soluble	Heavy	E-V-Q-L-V-G-S(SEQ ID NO:1)
Soluble	Light	D-I-Q-M-T-Q-S(SEQ ID NO:2)

Rituximab:

Rituximab Form	Antibody Chain	N-terminal sequence
Crystalline	Heavy	blocked
Crystalline	Light	Q-I-V-L-S-Q-S (SEQ ID NO:3)
Soluble	Heavy	blocked
Soluble	Light	Q-I-V-L-S-Q-S(SEQ ID NO:3)

The results show that the crystallization process does result in N-terminal amino acid degradation of the Trastuzumab or Rituximab antibodies.

Please delete paragraph [0322] on pages 115-118 and replace it with the following paragraph:

[0322] The following table summarizes Examples 44-46, 49, 50, 54, 53, 55 and 56, respectively, comparing the properties of native (soluble) and crystalline Rituximab:

Analytical Methods	Soluble	Crystalline	Result
<u>SDS-PAGE</u> non-reducing conditions	Whole Ab MW = ~ 150 kD	Whole Ab MW = ~ 150 kD	Soluble and crystalline forms of Rituximab were identical. Crystallization did not alter the structural integrity of Rituximab.
reducing conditions	H chain MW = ~ 50 kD L chain MW = ~ 25 kD	H chain MW = ~ 50 kD L chain MW = ~ 25 kD	
<u>HPLC gel filtration</u>	Single peak	Single peak	Crystallization did not alter the structural integrity of Rituximab.
<u>Dynamic Light Scattering</u>	MW = ~ 150 kD	MW = ~ 150 kd	Crystallization did not alter the structural integrity of Rituximab or change the hydrodynamic radius.
<u>Peptide mapping</u>	Trypsin digest	Trypsin digest	Similar profiles were obtained for soluble and redissolved Rituximab, indicating no change in conformation, structure or size

Analytical Methods	Soluble	Crystalline	Result
			of the Rituximab molecule.
<u>N-terminal Sequencing of Antibody Light Chains</u>	Gln-Ile-Val-Leu-Ser-Gln-Ser (SEQ ID NO: 3)	Gln-Ile-Val-Leu-Ser-Gln-Ser (SEQ ID NO: 3)	Native (soluble) and dissolved Rituximab had identical N-terminal sequences, indicating no hydrolysis of amino acids from the N-terminal side.
<u>Monosaccharide Constitution</u>	Fucose, mannose, N-acetyl glucosamine, galactose	Fucose, mannose, N-acetyl glucosamine, galactose	Native (soluble) and dissolved crystalline Rituximab had identical monosaccharide constituents, indicating that no monosaccharides were cleaved from the monoclonal antibody during crystallization.
<u>Oligosaccharide Profiling</u>	Three bands Corresponding to G8, G9 and G10, corresponding to 8-, 9-, and 10-residue sugars.	Three bands Corresponding to G8, G9 and G10, corresponding to 8-, 9-, and 10-residue sugars.	Native (soluble) and dissolved crystalline Rituximab had identical oligosaccharide profiles, indicating that crystallization does not alter the oligosaccharide make-up of the antibody.
Bioassays			Native and

Analytical Methods	Soluble	Crystalline	Result
Direct Cytotoxicity	Yes	Yes	dissolved Rituximab both induced each function. Thus, crystallization did not result in changes to immune functions.
Induced Complement Dependent Cytotoxicity	Yes	Yes	